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| 09/709,785 | 11/03/2000 | Anne N. Murphy | 660088.433C1 | 4280 |

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Stephen J Rosenman PhD
701 Fifth Avenue
Suite 6300
Seattle, WA 98104-7092

| EXAMINER | |
|---|---|
| CHAKRABARTI, ARUN K | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/709,785 | Applicant(s) Murphy |
|---|---|---|
| | Examiner Arun Chakrabarti | Art Unit 1655 |

-- **The MAILING DATE of this communication appears on the cover sheet with the correspondence address** --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on 1/13/01, 2/13/01, 6/1/01, 9/28/01, 10/12/01 and 11/18/01 .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 92-108 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 92-108 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4, 6
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

## DETAILED ACTION

### *Specification*

1. Applicant has elected method claims of Group IV corresponding to new claims 92-108. Accordingly, these claims are being examined.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 96, 104, 107 and 108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims are rejected over the use of the trademarks XPRESS and FLAG. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Moreover, MPEP 7.35.01 recites, "When a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson,* 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or

trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name." In the present case, the trademark or trade name is used to identify/describe the tags or labels of polypeptides and accordingly, the identification/description is indefinite.

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 92-94, 97-103 and 105 are rejected under 35 U.S.C. 103 (a) over Marban et al. (U.S. Patent 6,183,948 B1) (February 6, 2001) in view of Luban et al. (U.S. Patent 5,773,225) (June 30, 1998) further in view of Anderson et al. (U.S. Patent 6,140,067) (October 31, 2000).

Marban et al teach a method for screening for an agent that alters mitochondrial permeability transition (Abstract), comprising the steps of:

a) contacting a host cell comprising a mitochondrion with a candidate agent and an inducer of MPT (Abstract and Column 1, line 54 to column 2, line 20 and Claims 1, 17 and 18);

b) exposing the cell to an excitation energy (Column 14, lines 8-57);

c) detecting a level of energy transfer between the first and second energy transfer molecules (Column 14, lines 8-57 and Claims 1, 17 and 18); and

d) comparing the level of energy transfer to a first reference level generated in the absence of candidate agent, and therefrom identifying an agent that alters MPT (Figure 8 and Claims 1, 17 and 18).

Marban et al teach a method wherein the candidate agent increases or decreases energy transfer between the first and second energy transfer molecules (Figure 8 ).

Marban et al teach a method for altering survival of a cell and MPT, comprising contacting a mitochondrion with an identified agent, under conditions and for a time sufficient to alter MPT (Examples 1-4).

Marban et al do not teach a method wherein the host cell comprises (I) a first nucleic acid expression construct, comprising a promoter operably linked to a polynucleotide encoding a mitochondrial permeability transition pore component polypeptide fused to a polynucleotide encoding a first energy transfer molecule or a variant thereof, and (ii) a second nucleic expression construct, comprising a promoter operably linked to a polynucleotide encoding a cyclophilin

polypeptide fused to a polynucleotide encoding a second energy transfer molecule or a variant thereof, wherein binding of the mitochondrial permeability transition pore component polypeptide to the cyclophilin polypeptide results in detectable energy transfer between the first and second energy transfer molecules.

Luban et al. teach a method wherein the host cell comprises (I) a first nucleic acid expression construct, comprising a promoter operably linked to a polynucleotide encoding a first energy transfer molecule or a variant thereof, and (ii) a second nucleic expression construct, comprising a promoter operably linked to a polynucleotide encoding a cyclophilin polypeptide fused to a polynucleotide encoding a second energy transfer molecule or a variant thereof, wherein binding of the polypeptide to the cyclophilin polypeptide results in detectable energy transfer between the first and second energy transfer molecules (Figures 1-2 and Column 6, line 40 to column 9, line 25).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the cyclophilin D containing fusion protein of Luban et al. in the method for screening an agent that can alter MPT of Marban et al., since Luban et al. state, "The above assay can also be extended to assays using protein expressed in baculovirus, tissue culture cells or Gag purified from virus." ( Column 5, lines 22-24). An ordinary practitioner would have been motivated to combine and substitute the cyclophilin D containing fusion nucleic acid construct of Luban et al. in the method for screening an agent that can alter MPT of Marban et al in order to achieve the express advantages, as noted by Luban et

al., of an invention that can also be extended to assays using protein expressed in baculovirus, tissue culture cells or Gag purified from virus.

Marban et al in view of Luban et al do not teach nucleotide construct encoding a mitochondrial permeability transition pore component polypeptide fused to a polynucleotide wherein binding of the mitochondrial permeability transition pore component polypeptide to the cyclophilin polypeptide results in detectable energy transfer between the first and second energy transfer molecules.

Anderson et al teach a method for detecting an agent that alters mitochondrial permeability transition (Abstract and Claims 1-3 and 87).

Anderson et al teach cyclophilin D polypeptide and adenine nucleotide translocator polypeptide as mitochondrial membrane component which can naturally interact and bind to each other (Claims 23 and 91 and Column 3, lines 49-62).

Anderson et al teach the identification of an agent by comparing the altered mitochondrial function in presence and absence of the candidate agent (Claims 1-3).

Anderson et al teach a method for altering survival of a cell, comprising contacting a cell with an agent under conditions and for a time sufficient to modulate cell survival and alter MPT (Example 1).

Anderson et al do not teach a method of contacting a cyclophilin D polypeptide fusion protein with other protein.

Luban et al teach a method of contacting a cyclophilin D polypeptide fusion protein with other protein (Claims 1, 2 and 11).

Anderson et al do not teach a method wherein cyclophilin D polypeptide is immobilized on a solid support.

Luban et al teach a method wherein cyclophilin D polypeptide is immobilized on a solid support (Claim 6 and Column 16, lines 30-56).

Anderson et al do not teach a method wherein the fusion protein comprises a ligand for a receptor.

Luban et al teach a method wherein the fusion protein comprises a ligand for a receptor (Claims 7 and 8).

Anderson et al. teach nucleotide construct encoding a mitochondrial permeability transition pore component polypeptide fused to a polynucleotide wherein binding of the mitochondrial permeability transition pore component polypeptide to the cyclophilin polypeptide results in detectable energy transfer between the first and second energy transfer molecules (Claims 23 and 118 and Column 3, line 49 to Column 5, line 22). Moreover, Anderson et al teach cyclophilin D polypeptide and adenine nucleotide translocator polypeptide as mitochondrial membrane component which can naturally interact and bind to each other (Column 3, lines 49-63).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the mitochondrial permeability transition pore

component polypeptide of Anderson et al. in the method for screening an agent of Marban et al in view of Luban et al., since Anderson et al. state, "The present invention relates to improved screening assays for therapeutic agents useful in the treatment of type 2 diabetes mellitus, by comparing the levels of one or more indicators of altered mitochondrial function." (Abstract, lines 1-6). By employing scientific reasoning and in order to study the determinants of mitochondrial import which causes alteration of MPT, an ordinary practitioner would have been motivated to combine and substitute the the mitochondrial permeability transition pore component polypeptide of Anderson et al. in the method for screening an agent of Marban et al in view of Luban et al. in order to achieve the express advantages, as noted by Anderson et al., of an invention that relates to improved screening assays for therapeutic agents useful in the treatment of type 2 diabetes mellitus, by comparing the levels of one or more indicators of altered mitochondrial function such as MPT.

6. Claims 92-94, and 96-105 are rejected under 35 U.S.C. 103 (a) over Marban et al. (U.S. Patent 6,183,948 B1) (February 6, 2001) in view of Luban et al. (U.S. Patent 5,773,225) (June 30, 1998) further in view of Anderson et al. (U.S. Patent 6,140,067) (October 31, 2000). further in view of Briggs et al. (U.S. Patent 6,211,440 B1) (April 3, 2001).

Marban et al in view of Luban et al. further in view of Anderson et al. teach the method of claims 92-94, 97-103 and 105 as described above.

Marban et al in view of Luban et al. further in view of Anderson et al. do not teach the method wherein the energy transfer molecules are selected from green fluorescent protein (GFP).

Briggs et al. teach the method wherein the energy transfer molecules are selected from green fluorescent protein (GFP). (Column 42, lines 39-46).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the green fluorescent protein of Briggs et al. in the method to identify compounds affecting mitochondrial permeability of Marban et al. in view of Luban et al. further in view of Anderson et al. since Briggs et al. state, "Useful labels in the present invention include biotin for staining with labeled streptavidin conjugate, magnetic beads, fluorescent dyes (e.g., fluorescein, Texas Red, rhodamine, green fluorescence protein, and the like) (Column 42, lines 39-42)". By using the scientific reasoning and strong motivation provided by Briggs et al., an ordinary practitioner would have been motivated to combine and substitute the green fluorescent protein of Briggs et al. in the method to identify compounds affecting mitochondrial permeability of Marban et al in view of Luban et al. further in view of Anderson et al. in order to achieve the express advantages, as noted by Briggs et al., of useful label green fluorescence protein.

7. Claims 92-95, 97-103, and 105-106 are rejected under 35 U.S.C. 103 (a) over Marban et al. (U.S. Patent 6,183,948 B1) (February 6, 2001) in view of Luban et al. (U.S. Patent 5,773,225) (June 30, 1998) further in view of Anderson et al. (U.S. Patent 6,140,067) (October 31, 2000) further in view of Halestrap et al. (Biochimica et Biophysica Acta, (1998), Vol. 1366, pages 79-94).

Marban et al. in view of Luban et al. further in view of Anderson et al teach the method of claims 92-94, 97-103 and 105 as described above.

Marban et al. in view of Luban et al. further in view of Anderson et al do not teach the method, wherein the human cyclophilin A polypeptide is used.

Halestrap et al. teach the method, wherein the human cyclophilin A polypeptide is used (Page 80, Column 2, The molecular mechanism of the MPT Section, Subsection 2.1).

Marban et al. in view of Luban et al. further in view of Anderson et al do not teach the method, wherein the detection reagent is an antibody.

Halestrap et al. teach the method, wherein the detection reagent is an antibody.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the human cyclophilin A polypeptide and antibody detection reagent of Halestrap et al. in the method for screening an agent that can alter MPT of Marban et al. in view of Luban et al. further in view of Anderson et al , since Halestrap et al. state, "We discuss how the MPT may be involved in determining whether cell death occurs by necrosis or apoptosis. (Abstract, last sentence)". Moreover, Anderson et al teach cyclophilin D polypeptide and adenine nucleotide translocator polypeptide as mitochondrial membrane component which can naturally interact and bind to each other. An ordinary practitioner would have been motivated to combine and substitute the human cyclophilin A polypeptide and antibody detection reagent of Halestrap et al. in the method for screening an agent that can alter MPT of Marban et al. in view of Luban et al. further in view of Anderson et al in order to

achieve the express advantages, as noted by Anderson et al., of an invention that relates to improved screening assays for therapeutic agents useful in the treatment of type 2 diabetes mellitus, by comparing the levels of one or more indicators of altered mitochondrial function. And also to elucidate how the MPT may be involved in determining whether cell death occurs by necrosis or apoptosis.

***Conclusion***

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Kr. Chakrabarti

**Arun Chakrabarti**
**Patent Examiner**
**Art Unit 1655**

**January 9, 2002**